



# Biosciences and Biotechnology

Protecting the nation by countering current and future biological and environmental threats.

## Security: Health and Energy

Bioscience and biotechnology research at Lawrence Livermore National Laboratory (LLNL) delivers transformative biological solutions for the security needs of the nation. Integrated, multidisciplinary teams of biologists and bioengineers combine experimental and computational approaches for making scientific discoveries and developing innovative technologies.

Bringing together state-of-the-art capabilities and partnerships in quantitative biology, computing, and precision measurement, Laboratory bioscientists provide early biological threat assessment and accelerated drug discovery and vaccine development. Extending biological models to include climate and ecology research, LLNL researchers provide innovative solutions for biofuels, carbon storage in soils, and biomining of critical minerals. They also develop bio-enhanced manufacturing processes for biomaterials.

The ability to deliver innovative solutions is supported by a deep understanding of complex biological systems and microbial communities, scientific discoveries, and cutting-edge capabilities. Integrating state-of-art analytical capabilities, synthetic biology techniques, and high-performance computing, Laboratory staff evaluate the mechanisms of disease and engineer microbial communities to counter biosecurity, health, and ecological threats.

## Accomplishments

LLNL is one of the few places in the nation focused on coupling multidisciplinary biological expertise with world-class resources in high-performance computing and unique experimental facilities to solve health and environmental problems of national importance. Emerging areas of research include microbiome engineering for health, energy, and the environment; rapid response to the emergence of novel pathogens; and the development of diagnostics and treatment approaches for cognitive impairment.

Examples of LLNL bioscience and biotechnology achievements:

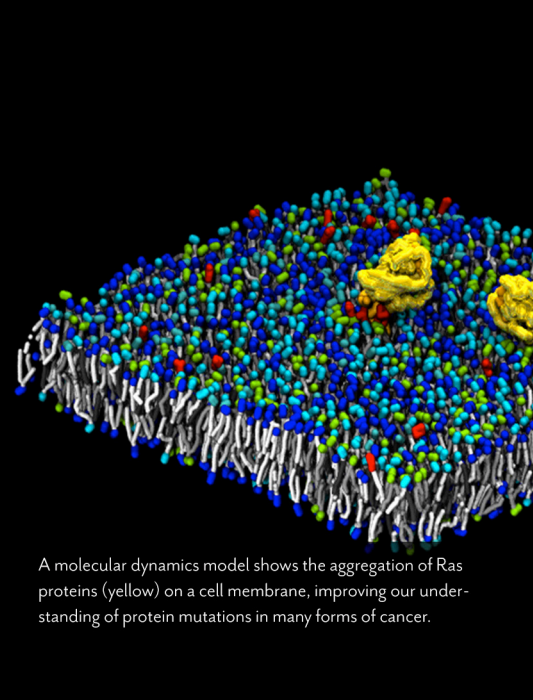
- LLNL researchers designed the Lawrence Livermore Microbial Detection Array, a pangenomic platform for rapid detection of more than 12,000 microorganisms within a day. It is now used for applications as diverse as biodefense, drug and food safety, and space biology.
- Integrated computational and experimental efforts led to the development of the LLNL therapeutic antibody design platform. With this platform, experts were able to revive an approved COVID-19 therapy that had lost effectiveness and use it to combat the Omicron variants.
- LLNL's nanoparticle-based vaccine delivery platform advances vaccine development for human health and biosecurity pathogens. Novel vaccine formulations are being tested in animals for their ability to protect against chlamydia and other pathogen infections.
- Laboratory bioscientists are accelerating drug discovery and development by combining physics-based modeling and simulation platforms with machine-learning algorithms.
- Livermore researchers detected microbial signatures that inform the treatment of wounds from combat injuries in soldiers using a combination of microbial metagenomic DNA sequencing and machine learning.
- LLNL bioscientists developed sustainable biomining approaches for the extraction and purification of rare-earth elements to ensure the domestic supply of critical minerals for the clean-energy transition.



LLNL's in vitro chip-based human investigational platform accelerates drug discovery. The heart-on-a-chip, rendered here, measures the effects of various compounds on human heart cells.



Researchers Nick Fischer and Amy Rasley characterize nanolipoprotein particle vaccine formulations (crucial for vaccine development) using a dynamic light-scattering instrument.



A molecular dynamics model shows the aggregation of Ras proteins (yellow) on a cell membrane, improving our understanding of protein mutations in many forms of cancer.

## Scientific Underpinning

Multidisciplinary teams of scientists and engineers combine biological science, high-performance computing, and precision measurement and engineering to understand, predict, and engineer the behaviors of complex biological systems. By coupling world-class computational resources with targeted experiments, the Laboratory applies the central principles of the design–build–test–learn cycle to engineer biological molecules and systems with the desired functionality.

Some examples of cutting-edge capabilities include:

- High-performance computing to simulate biological systems at various scales, including atomistic and coarse-grained molecular dynamics; quantum simulations; constraint-based genome-scale simulations; reaction–transport dynamic simulations; and agent-based, whole-organ, and pharmacokinetic and pharmacodynamic models.
- The National User Resource for Biological Accelerator Mass Spectrometry, the only user resource of its type in the United States, which provides ultra-high-sensitivity quantitative isotopic analysis for biomedical researchers measuring extremely low concentrations of radioisotopes.
- Experimental and computational platforms for the blood–brain barrier and central nervous system that can be broadly used for biological and chemical threat analysis and therapeutic development.
- A combination of stable isotope probing, advanced imaging, proteogenomic profiling, and computational modeling, which is used to probe microbial communities within their ecological context.
- Synthetic biology techniques and secure biosystems design for engineering safe and effective microorganisms and communities for environmental applications and medical countermeasures.
- A Select Agent Center, which is the only Biosafety Level-3 laboratory in the U.S. Department of Energy national laboratory complex; additive manufacturing with bioprinting and biomaterials expertise; and forensic sciences capabilities at the Laboratory's Forensic Science Center.

## The Future

Bioscience and biotechnology researchers are targeting the following challenges to address pressing issues in disease prevention, ecosystem sustainability, and biomanufacturing:

- Providing early biological threat assessment and accelerating the development of countermeasures to human exposures and disease, including next-generation diagnostic and surveillance systems, broad-target antibodies, and novel therapeutics and vaccines.
- Expanding our understanding of cellular mechanisms and the interaction among cells, both within tissues and within communities to inform genotype-to-phenotype predictions and genome engineering strategies to combat disease and develop biomaterials.
- Designing and engineering nanostructured materials and advanced characterization tools for national security applications.